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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/866,066 | 05/25/2001 | Christopher W. Benjamin | 0229US1/PHRM-0328 | 6862 |

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| EXAMINER | |
|---|---|
| WEGERT, SANDRA L | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1647 | |

DATE MAILED: 04/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/866,066 | BENJAMIN ET AL. | |
| | Examiner | Art Unit | |
| | Sandra Wegert | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-30,32,33,35-73 and 76-115* is/are pending in the application.

4a) Of the above claim(s) *1-29,36-73,78-88 and 95-115* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30,32,33,35 and 89-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### Status of Application, Amendments, and/or Claims

The amendment filed 3 November 2003 has been entered. Claims 1-29, 36-73,78-88 and 95-115 are withdrawn. Claims 31, 34, 74 and 75 are canceled. Claims 30, 32, 33, 35 and 89-94 are under examination. Claim 35 was inadvertently listed as withdrawn in one section of the previous Office Action (page 2, 20 May 2003).

The text of those sections of Title 35, U.S. Code not included in this action can be found in a previous Office action.

### *Withdrawn Objections and/or Rejections*

***Title***

The objection to the title as set forth at page 3 of the previous Office Action (20 May 2003) is *withdrawn* in view of the amendment which introduced a new title (3 November 2003).

***URL's***

The objection to the specification because it contained browser-executable code, as set forth at page 3 of the previous Office Action (20 May 2003), is *withdrawn* in view of the amendment which removed all hypertext links from the disclosure (3 November 2003).

***Claim Objections***

The objection to Claims 31-34,74, 75 and 90-93 for reciting non-elected subject matter (page 4, 20 May 2003), is *withdrawn*. Applicants amended Claims 31-34,74 and 75 to remove references to SEQ ID NO: 21-38 (3 November 2003).

The objection to Claims 30 and 89 are objected to for depending from non-elected claims (page 4, 20 May 2003), is *withdrawn*. Applicants amended Claims 30 and 89 to remove dependency from non-elected Claims (3 November 2003).

***Claim Rejections - 35 USC § 112, second paragraph-indefiniteness.***

The rejection of Claims 32, 33 and 92 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for reciting the phrases: "an amino acid sequence homologous to a sequence" or "at least one conservative amino acid substitution" (20 May 2003), is *withdrawn.* Applicants amended Claims 32 and 33 to remove the phrases (3 November 2003).

***Maintained Objections and/or Rejections***

The objection to Claims 90-93 for reciting non-elected subject matter (page 4, 20 May 2003), is *maintained.* Applicants amended Claims 31-34,74 and 75 to remove references to SEQ ID NO: 21-38 (3 November 2003), but did not amend Claims 90-93.

***35 U.S.C. § 101/112, first paragraph-, Lack of Utility, Enablement.***

Claims 30, 32, 33, 35 and 89-94 are rejected under 35 U.S.C. 101, as lacking utility. The

reasons for this rejection under *35 U.S.C. § 101* are set forth at pp. 4-12 of the previous Office Action (20 May 2003). Claims 30, 32, 33, 35 and 89-94 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office Action (20 May 2003), one skilled in the art clearly would not know how to use the claimed invention.

The claims are directed to a nucleotide that encodes a protein that possesses approximately 2-30% homology to known proteins, such as that encoded by part of clone RP11-661h17 (2003, DOE Joint Genome Institute, Accession No. AC138924, see residues 8929-9550), or a portion of Drosophila potassium channel protein Locus T13807 (2000, Goldstein, et al Accession No. T13807), or Arabidopsis protein T27I1.1 (1999, Federspiel, et al, Accession No. T00618). As discussed in the previous Office Action (page 5), no well-established utility exists for newly isolated complex biological molecules. The specification does not disclose experiments that impart *any* specific function for the claimed polypeptide in the context of the cell or organism. The specification does not teach the skilled artisan how to use the channel peptide for any unique or specific purpose. Nor does the specification predict or discuss a specific function for the disclosed polynucleotide. For example, there is no disclosure of the use of substrates for the channel, or changes in channel-mediated processes in transfected cells, or the phenotypes of "knock-in" or "knock-out" organisms, or of patch-clamp assays, or of diseases caused by an overactivity or underactivity of the channel. The skilled artisan is not provided with sufficient guidance to use the claimed polypeptide for any purpose.

It is noted that at pages 24-41 of the Response, the Applicant cites pertinent case law reviewing the current legal standards of *Utility*. The Examiner takes no issue with Applicant's general comments regarding the legal standard for Utility of novel inventions. Issues pertinent to utility of the instant invention, however, receive comment below:

Applicants argue (page 28, 20 May 2003) that the nucleotides of the instant Specification encode ion channels. Thus, "[b]ecause all ion channels, as a class, convey practical benefit (much like the class of DNA ligases identified in the Training Materials), there should be no need to provide additional information about them" (page 28, middle paragraph). However, the disclosed polynucleotides of the Instant Specification and the claimed polypeptide are currently unidentified molecules. Very little information is given in the Specification about specific substrates or ligands of the polypeptide encoded by the claimed polynucleotide(s), or of disease states due to mutant polynucleotides. The Specification suggests that the disclosed polynucleotide is an ion channel: "*Homologous amino acid sequences include those amino acid sequences which contain conservative amino acid substitutions in SEQ ID NO:20 to SEQ ID NO:38, as well as polypeptides having ion channel activity*" (paragraph 52), and "*A preferred polynucleotide has a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:19, which correspond to naturally occurring ion-x sequences*" (paragraph 73). However, the closest homologies detected when searching the disclosed nucleotide against public gene databases is to an unidentified portion of chromosome 16 clone RP11-661h17. The claimed polypeptide's homology to ion channels is approximately 1-10%. Even if the disclosed polynucleotide were shown to encode an ion channel family member, further evidence of a

function specific to the claimed polypeptide or disclosed nucleotide would be needed, since, unlike DNA ligases, the ion channel family is large and functionally diverse (IUPHAR subcommittee, 1997, TIPS 18:76-84; Warmke and Ganetzky, 1994, PNAS, 91: 3438-3442; Lehmann-Horn and Jurkat-Rott, 1999, 79(4): 1317-1372, for example).

Applicants imply (page 26, for example) that the courts have defined Utility requirements more broadly than those applied in examination of the current Application, for example in Brenner v. Manson (148 USPQ 689), Anderson v Natta, 480 F.2d 1392, 1397 (CCPA 1973), Juicy Whip Inc.v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999) and Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984).

Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons:

The fact patterns of Anderson v Natta, 480 F.2d 1392, 1397 (CCPA 1973), Juicy Whip Inc.v. Orange Bang Inc., 51 USPQ2d 1700 (Fed. Cir. 1999), Envirotech Corp. v. Al George, Inc., 730 F.2d 753, 762, 221 USPQ 473, 480 (Fed. Cir. 1984) are significantly different than those in the current Utility Guidelines (Federal Register, 2001, 66: 1092-1099). The cited court decisions are therefore not significant or binding with regard to the instant rejections.

Brenner v. Manson (383 US 519), however, *did* contemplate the utility of new inventions and concluded:

"The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field (Justice Fortas, writing for the majority)."

As stated in the conclusion: "A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion (Fortas)."

Applicants have not indicated or predicted a substantial or specific utility for the disclosed polynucleotide or claimed polypeptide. Furthermore, since the claimed polypeptide has very low homology to known channels, homology or relatedness cannot be used to assign utility to the claimed polynucleotide.

Applicants also discuss Nelson v Bowler (206 USPQ 881, 1980) as support for the contention that their invention has a "substantial" utility (page 29, 3 November 2003). However, the case of Nelson v Bowler only contemplates the degree of certainty required of experimental evidence submitted in support of a contended utility and that, furthermore, the data need not point to treatment of human diseases. The Court ruled that a showing of practical utility for a composition may be satisfied by an adequate showing of any pharmacological activity, without a showing of direct therapeutic utility. Thus, the identification of some specific pharmacological activity of a compound that is relevant to an asserted pharmacological use provides an "immediate benefit to the public" and thus satisfies the utility requirement. See MPEP 2107 (III). The conclusions are that an invention need not have a therapeutic value, and the applicant need not prove that the utility is true "beyond a reasonable doubt." As discussed above, the instant specification does not suggest a specific function for the claimed polynucleotide- indeed the disclosed polynucleotide and claimed polypeptide have not been identified- so the believability of submitted evidence is not a critical issue in patentability of the claimed polynucleotide.

Applicants contend that they have demonstrated a "substantial likelihood" of utility by showing a "reasonable correlation" between the utility of the known composition and the composition being claimed, and cite: In re Cortwright, 165 F.3d at 1356; Brana, 51 F.3d at 1566,

In re Langer, 503 F.2d 1380, 1391-92 (CCPA1974) and Fujikawa v. Wattanasin, 93 F.3d 1559, 1565 (Fed. Cir.1996). Applicants go on: "The presently claimed ion channel is related to known ion channels. The Office has not provided evidence or sound scientific reasoning that one skilled in the art would doubt the "reasonable correlation" advanced by Applicants. Accordingly, under Brana, the Patent Office must accept the utility asserted by Applicants.

Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons:

Except perhaps for *Fujikawa v Wattanasin*, the fact patterns of the cases cited by the Applicant are significantly different than those discussed in the current Office Action. The cited court decisions are therefore not significant or binding with regard to the instant rejections. The case of *Fujikawa v Wattanasin* centered on species of novel mevalonolactones, chemical compounds with structures somewhat like steroids. The claimed invention was a method of inhibiting the biosynthesis of cholesterol by administering to patients an appropriate dose of a compound falling within the scope of the genus of mevalonolactones. What makes this case irrelevant to examination of the instant Application is that a well-described species of a genus of simple *chemical structures* may well have utility based upon its homology to other members of a class. For novel polypeptides, however, this is seldom the case. As the Utility Guidelines (Federal Register, 2001, 66: 1092-1099) go on to say in the discussion of *Fujikawa v Wattanasin,* "where a class of proteins is defined by common structural features, but evidence shows that the members of the class do not share a specific, substantial functional attribute or utility, despite having structural features in common, membership in the class may not impute a specific, substantial, and credible utility to a new member of the class. When there is a reason to doubt the

functional protein assignment, the utility examination may turn to whether or not the asserted protein encoded by a claimed nucleic acid has a well- established use. If there is a well-established utility for the claimed protein and the encoding nucleic acid, the claims would meet the requirements for utility under 35 U.S.C. 101. If not, the burden shifts to the applicant to provide evidence supporting a well-established utility. *There is no per se rule regarding homology, and each application must be judged on its own merits."* (italics added).

To address the comparison of the Instant Application to prior Patents, as listed on pages 34-35 (3 November 2003): The current rejection is in compliance with the most currently-published version of the Utility Guidelines, which require that all biological inventions must have credible, specific and substantial utility. Additionally, each Patent Application is examined on its own merits. What was deemed allowable in one Patent has no bearing on this Application. Furthermore, it should be pointed out that post-filing date evidence of Utility, submitted during prosecution of a Patent Application, seldom finds its way into a US Patent. In other words, the issued Patents themselves reveal nothing about their prosecution.

There is no evidence that the protein disclosed in the instant Specification is related to ion channels. However, even if it were established as such, additional specific functional assays would be needed since these families of proteins are very large and enormously varied, as described above. Often, even closely-related family members sometimes work very differently and have different specific functions in the organism. The examples given above and others demonstrate that one skilled in the art would not know the utility and function of the polypeptide disclosed in the instant disclosure, even if it *were* classified as an ion channel because, as

discussed in the related art above and the specification of the instant application, ion channels have many uses and are involved in countless disorders and diseases:

"ion channels may be useful targets for discovering ligands or drugs to treat many diverse disorders and defects, including schizophrenia, depression, anxiety, attention deficit hyperactivity disorder, migraine, stroke, ischemia, and neurodegenerative disease such as Alzheimer's disease, Parkinson's disease, glaucoma and macular degeneration. In addition compounds which modulate ion channels can be used for the treatment of cardiovascular diseases including ischemia, congestive heart failure, arrhythmia high blood pressure and restenosis" (Specification, paragraph 21).

Proper analysis of the Wands factors were provided in the previous Office Action. Due to the large quantity of experimentation necessary to determine an activity or property of the claimed polypeptide such that it can be determined how to use the claimed polypeptide or disclosed polynucleotide encoding the ion channel-like polypeptide and to screen for activity, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot be predicted based on structural similarity, the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite particular biological activities, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

***35 U.S.C. 112, first paragraph- Written Description***

Claims 34, 74, 75 and 93 are rejected under 35 U.S.C. 112, first paragraph, for reasons of record (pages 12-14, 20 May 2003). Applicants have not addressed the *Written Description* rejection in their arguments presented 3 November 2003.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

***Advisory information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached at (571) 272-0887.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

SLW

4/13/04

ELIZABETH KEMMERER
PRIMARY EXAMINER